# PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

# PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| | Date of mailing *(day/month/year)* |
| Applicant's or agent's file reference<br>B030487BQH21 | FOR FURTHER ACTION<br>See paragraph 2 below |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/JP2004/016485 | 29.10.2004 | 28.11.2003 |

International Patent Classification (IPC) or both national classification and IPC

Applicant
KANEKA CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| Name and mailing address of the ISA/JP | Authorized officer |
|---|---|
| Facsimile No. | Telephone No. |

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016485

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016485

**Box No. III** Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 10, 11, 22

because:

☒ the said international application, or the said claims Nos. 10, 11, 22 relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 10, 11 and 22 relate to a method for treatment of the human body by therapy.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 10, 11, 22

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/016485

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 5-7, 17-19 | YES |
| | Claims | 1-4, 8, 9, 12-16, 20, 21 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-9, 12-21 | NO |
| Industrial applicability (IA) | Claims | 1-9, 12-21 | YES |
| | Claims | | NO |

2. Citations and explanations:

The following documents are given in the International Search Report.

Document 1: JP 2003-26625 A, 29 January 2003
Document 2: JP 2003-119127 A, 23 April 2003
Document 3: Free Radical Biology & Medicine, 1990, Vol. 9, pp. 117-126
Document 4: Biol. Pharm. Bull., 1996, Vol. 19, Number 8, pp. 1005-1012
Document 5: Hiroshima Daigaku Igaku Zasshi, 1993, Vol. 41, No. 6, pp. 417-427
Document 6: Redox Report, 1995, Vol. 1, Number 5, pp. 343-347
Document 7: JP 2003-104945 A, 09 April 2003
Document 8: JP 10-109933 A
Document 9: JP 9-187229 A
Document 10: JP 2003-306429 A, 28 October 2003
Document 11: Research Communications in Pharmacology and Toxicology, 1999, Vol. 4, No. 3 & 4, pp. 163-170
Document 12: Nihon Igaku Daigaku Zasshi, 1995, Vol. 62, No. 3, pp. 271-282
Document 13: WO 2000/057871 A2

(1) Novelty and inventive step of claims 1-4, 8 & 9 (documents 1, 2)

Documents 1 and 2 describe food, animal feed and other compositions containing the reduced coenzymes Q1 through Q12 (document 1, claims 1 & 23, document 2, claims 1, 3, 8, 12).

(2) Inventive step of claims 1-3 & 5 (documents 3, 4)

Document 3 describes that the reduced coenzymes Q1-Q10 suppress lipid hyperoxidation in the liver through an antioxidation effect (page 119, Figure 1C, page 121, Figure 4, etc.).

In the invention of this application, liver function protection appears to mean suppressing lipid hyperoxidation in the liver (Example 1 of the invention of this application and document 4, page 1010, lower left column).

Consequently, using the reduced coenzymes Q1-Q10 as liver function protection drugs would be an obvious matter to a person skilled in the art by taking into consideration the descriptions of documents 3 and 4.

(Continued)

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

(3) Inventive step of claims 1-3 & 5 (documents 5-8)

Documents 5 and 6 describe that the reduced coenzyme Q10 produced by reduction in the liver of the administered oxidized coenzyme Q10 exhibits an antioxidation effect and inhibits liver function disorder (document 5, page 421, left column, line 4 to page 422, right column, line 6 & page 422, Tables 1 and 2, document 6, page 345, right column, lines 10-18, etc.).

Consequently, using the reduced coenzyme Q10 as a liver function protection drug would be an obvious matter to a person skilled in the art.

Here, whether the reduced coenzyme Q10 exhibits a better liver function protection effect than the oxidized form when administered orally is examined. Document 3 describes that the reduced coenzyme Q10 has a better antioxidation effect in the liver than the oxidized form (page 119, Figure 1C, page 120, left column, lines 10-13), while document 7 describes that of the oxidized coenzymes Q, only some are reduced and have an antioxidation effect in the body (paragraphs 0003-0005). Moreover, document 8 describes that the reduced coenzyme Q10 has better oral absorption than the oxidized form (Examples 1 & 2, Figures 1 & 2). Thus, the liver function protection effect of the invention of this application is not remarkable but is attributable merely to efficient supply of the reduced coenzyme Q10, which has a better antioxidation effect and hence a better liver function protection effect than the oxidized coenzyme Q10.

(4) Inventive step of claims 6, 7 (documents 1-8)

In addition to the points made in (2) and (3) above, documents 1 and 2 describe the use of the reduced coenzymes Q1-Q12 as drugs in capsule and other forms, so appropriately changing the formulation of reduced coenzymes Q1-Q10 would be an obvious matter to a person skilled in the art (descriptions of documents 1 & 2 mentioned under (1) above, paragraph 0030 of document 1).

(5) Novelty and inventive step of claims 12-16, 20 & 21 (documents 2, 9, 10)

Documents 2, 9 and 10 describe food, animal feed and other compositions containing the reduced coenzymes Q1-Q12 (description of document 1 mentioned under (1.1), Claim 1 and paragraph 0008 of document 9, claims 1, 4 and 7 and paragraph 0008 of document 10).

(6) Inventive step of claims 12-19 (documents 2, 11-13)

Documents 11 and 12 describe that liver function disorder can be inhibited by oral administration of the oxidized coenzyme Q10 in mice with liver function disorder induced by carbon tetrachloride or endotoxin (document 11, table 1, figures 1 & 2, document 12, figures 2 & 3, etc.).

Moreover, document 3 describes that when administered orally and in various other forms, the oxidized coenzymes Q1-Q12 are effective against diseases stemming from liver disorder, hepatitis B and other forms of oxidation disorder (claims 1 & 11, page 18, line 19 to page 19, line 34, page 22, lines 25-32, etc.).

Consequently, since document 2 describes the use of the oxidized coenzymes Q1-Q12 as drugs in capsule and other forms, appropriately changing the formulation of the oxidized coenzymes Q1-Q12 would be an obvious matter to a person skilled in the art (see the description of document 2 given under (1)).